

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Christensen, Leif
Frydenlund Hansen, Henrik
Nielsen, Peter E
- (ii) TITLE OF INVENTION: Substituted Nucleic Acid Mimics
- (iii) NUMBER OF SEQUENCES: 10
- (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Woodcock Washburn et al.
(B) STREET: One Liberty Place 46th Floor
(C) CITY: Philadelphia
(D) STATE: PA
(E) COUNTRY: USA
(F) ZIP: 19103
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: US/08/612,661
(B) FILING DATE: 08-MAR-1996
(C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Caldwell, John W
(B) REGISTRATION NUMBER: 28,937
(C) REFERENCE/DOCKET NUMBER: ISIS-2169
- (ix) TELECOMMUNICATION INFORMATION:
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(B) TELEFAX: 215-568-3439

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 10 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: YES
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

AAAAGGAGAG

10

(2) INFORMATION FOR SEQ ID NO:2:

- (i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 17 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: YES
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

GAGAGGAAAA

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(2) INFORMATION FOR SEQ ID NO:3:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 base pairs
 - (B) TYPE: PNA
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

TTTTCCTCTC

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(2) INFORMATION FOR SEQ ID NO:4:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 base pairs
 - (B) TYPE: PNA
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

TTTTCNTCTC

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(2) INFORMATION FOR SEQ ID NO:5:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 10 base pairs
 - (B) TYPE: PNA
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

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cont

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

TTTTCNTNTC

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(2) INFORMATION FOR SEQ ID NO:6:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 10 base pairs
 (B) TYPE: PNA
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

TTTTNNTCTC

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(2) INFORMATION FOR SEQ ID NO:7:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 10 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

GTAGGTCCT

10

(2) INFORMATION FOR SEQ ID NO:8:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 10 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

GTAGATCACT

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(2) INFORMATION FOR SEQ ID NO:9:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 10 base pairs
 (B) TYPE: PNA
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

AGTCACCTAC

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(2) INFORMATION FOR SEQ ID NO:10:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 10 base pairs
 (B) TYPE: PNA
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: PNA

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

AGTCANCTAC

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Subcloned

DOCKET NO.: ISIS-2169

PATENT

Page 20, line 15, at the end of the line, insert -- SEQ

a1 ID NO:4, where C^{Bz} is N --

Page 20, line 16, at the end of the line, insert -- SEQ

a2 ID NO:5, where C^{Bz} is N --

Page 20, line 17, at the end of the line, insert -- SEQ

a3 ID NO:6, where C^{Bz} is N --

Page 22, line 8, at the end of the line, insert -- SEQ

ID NO:7 --

Page 22, line 9, at the end of the line, insert -- SEQ

ID NO:8 --

Page 22, line 11 at the end of the line, insert -- SEQ

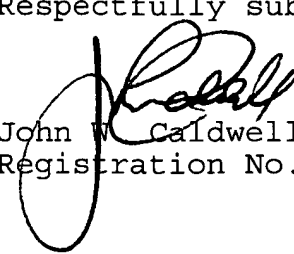
ID NO:9 --

Page 22, line 12 at the end of the line, insert -- SEQ

a4 ID NO:10, where C^{Bz} is N --

Applicants respectfully request consideration and allowance of all pending claims. Early and favorable notification to that effect is earnestly solicited.

Respectfully submitted,


John W. Caldwell
Registration No. 28,937

May 24 1984
Date:
WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS
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ISIS-2169

each R^1 and R^2 is independently selected from the group consisting of hydrogen, (C_1-C_4) alkyl which may be hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen;

each of G^1-G^{n-1} is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

Q is $-CO_2H$, $-CONR'R''$, $-SO_3H$ or $-SO_2NR'R''$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

I is $-NHR'''R''''$ or $-NR'''C(O)R''''$, where R' , R'' , R''' and R'''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups, reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

12. The nucleic acid mimic according to claim 11 wherein said target molecule is a nucleic acid.

13. The nucleic acid mimic according to claim 11 wherein said sterically bulky substituent is $-R'$, $-OR'$, $-SR'$, $-N(R')_2$, $-C(R')_3$, $-C(=X)(R')$, $-C(=X)(-Y-R')$ or $S(=O)_{1-2}(-Y-R')$ wherein:

X is O, S or NH;

Y is O, S or NH; and

R' comprises at least 3 atoms and is H, C_1-C_{50} -alkyl, C_2-C_{50} -alkenyl, C_2-C_{50} -alkynyl, C_7-C_{50} -alkyl-aryl, C_6-C_{50} -aryl, $C_{10}-C_{50}$ -

ISIS-2169

naphthyl, C₁₂-C₅₀-biphenyl, C₇-C₅₀-aryl-alkyl, pyridyl, imidazolyl, pyrimidinyl, pyridazinyl, quinolyl, acridinyl, pyrrolyl, furanyl, thienyl, isoxazolyl, oxazolyl, thiazolyl and biotinyl, wherein R' can be substituted one or more times by -NO, -NO₂, -SO₃⁻, -CN, -OH, -NH₂, -SH, -PO₃²⁻, -COOH, -F, -Cl, -Br and -I.

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14. The nucleic acid mimic according to claim ~~11~~⁴ wherein said base is a naturally or non-naturally occurring pyrimidine base.

15. The nucleic acid mimic according to claim ~~14~~⁵ wherein said sterically bulky substituent is bound to C-6, C-5 or N-4 of said naturally occurring pyrimidine base.

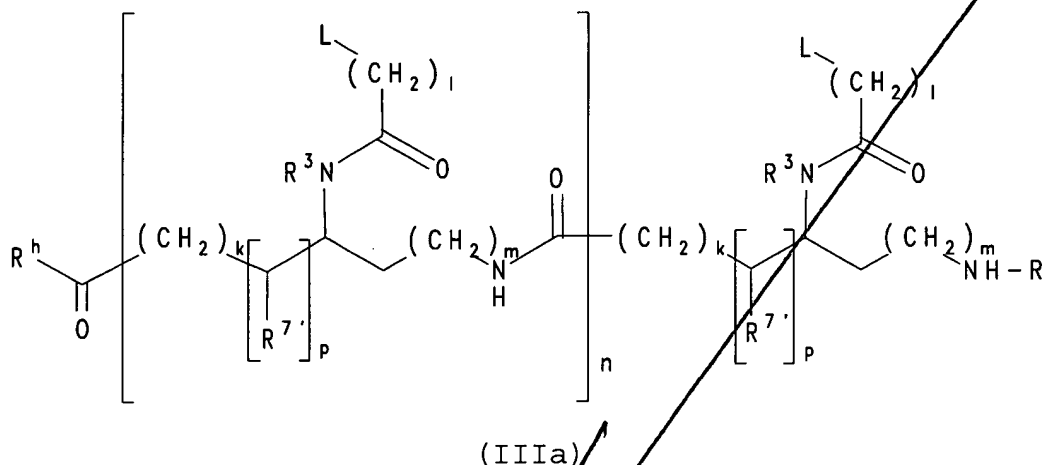
16. The nucleic acid mimic according to claim ~~15~~⁶ wherein said sterically bulky substituent is bound to N-4 of said naturally occurring pyrimidine base.

17. The nucleic acid mimic according to claim ~~16~~⁷ wherein said naturally occurring pyrimidine base is cytosine.

18. The nucleic acid mimic according to claim ~~16~~⁸ wherein said sterically bulky substituent is (C=O)-R'' wherein R'' is C₁-C₂₀-alkyl or C₆-C₁₈-aryl.

19. The nucleic acid mimic according to claim 18 wherein said sterically bulky substituent is $(C=O)-C_6H_5$.

20. The nucleic acid mimic according to claim 11 having formula (IIIa):



wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic base moieties, including those substituted with a sterically bulky group or groups, naturally occurring nucleobases, and non-naturally occurring nucleobases, at least one L being said base substituted with at least one sterically bulky substituent;

each R^{7'} is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60;

each of k, l, and m is independently zero or an integer from 1 to 5;